SILOXANE CONTAINING MACROMONOMERS AND DENTAL COMPOSITES THEREOF

Related Applications

[0001] This application is a continuation of Serial Number 10/213,050 filed August 6, 2002 (Case KON-76 2CON) which claims the benefit of Serial Number 09/626,200 filed July 26, 2000 (Case KON-76) which claims the benefit of U.S. Provisional Application Serial Number 60/146,093 filed July 28, 1999 (Case KON-76 PRO).

Technical Field

[0002] This invention relates to siloxane containing macromonomers and dental composites thereof.

Background of the Invention

[0003] In the last decade dental restorative materials, especially dental composites, becomes a high interest. Manly the aesthetic quality of the filling material should be improved in comparison to amalgam and a possible toxicological risking should be avoided.

[0004] Presently, commercial dental composites exhibit outstanding mechanical properties, such as compressive strengths ranging from 300 to 500 MPa and flexural strengths ranging from 130 to 170 MPa. Furthermore, over the past years they have been improved with respect to abrasion resistance, marginal integrity, fatigue behavior and their optical properties. Nevertheless, a volumetric shrinkage of about 2.5 to 4.0% takes place during the polymerization of these composites. This shrinkage may lead to marginal gap formation, microfractures in the material and sometimes enamel edge cracks. Secondary caries may arise as a result of these defects. Therefore an important objective is to develop new composite materials that exhibit reduced volumetric shrinkage without sacrificing other beneficial properties.

[0005] The volumetric shrinkage is influenced by two different effects: firstly, during polymerization the van der Waals distance of the monomers are replaced by covalent bonds and secondly, the packing density of the polymers increases in comparison to that of the monomers. There are several possibilities to reduce the volumetric shrinkage.

[0006] In order to reduce volumetric shrinkage and improve mechanical properties materials that comprises polymerizable moieties and additionally siloxane groups were proposed in the past years. Organosiloxanes described by prior art are mono (meth)acrylates having one siloxane moiety (US 5192815), polyfunctional compounds as well as the so-called ORMOCER® materials (DE 3903407, DE 4133494). Due to the relatively high viscosity of these materials they are only usable in combination with reactive diluents. It is well-known that low-molecular methacrylates are less or non biocompatibility and have a relatively high volumetric shrinkage.

[0007] An aim of the invention was to reduce shrinkage by partial or complete replacement of low-molecular polymerizable monomers by the novel siloxane comprising macromonomers.

Brief Description of the Drawings

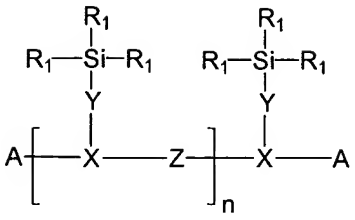
[0008] Fig. 1 - Transmission electron microscopic photograph of nano-scaled particles

[0009] Fig. 2 - Transmission electron microscopic photograph of nano-scaled particles

[0010] Fig. 3 - Element specific image - TEM image of the acid catalyzed condensation product (film on carbon-grid

Preferred embodiments of the invention

[0011] The invention concerns macromonomers of a molecular weight of at least $M \geq 500$ g/mol containing at least one siloxane group that are described by the following generally formula:



wherein

A is a polymerizable moiety, preferably an olefinic double bond, most preferably acrylate or methacrylate,

R_1 is an C_1 to C_{18} oxyalkyl, a C_5 to C_{18} oxycycloalkyl or a C_5 to C_{15} oxyarylene, C_1 to C_{18} alkyl, a C_5 to C_{18} cycloalkyl or a C_5 to C_{15} arylor heteroaryl

X is N or a substituted or unsubstituted C_1 to C_{18} alkylene, a C_1 to C_{18} oxyalkylene or C_1 to C_{18} carboxyalkylene

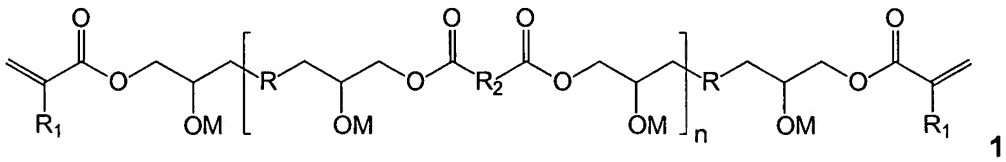
Y is an C_1 to C_{18} alkylene, C_1 to C_{18} oxyalkylene or an urethane -O-CO-NH- linking moiety

Z is an C_1 to C_{18} alkylene, a C_5 to C_{18} cycloalkylene or a C_5 to C_{15} arylene or heteroarylene,

n is an integer.

[0012] The dental/medical composite is usable as a dental restorative material for filling and restoring teeth, making inlays and onlays, as core build-up materials, for artificial teeth, for sealing and coating materials, usable as temporary crown and bridge material.

[0013] Examples of the used macromonomers containing alkoxysilyl groups are given in formulas **1** to **15**.



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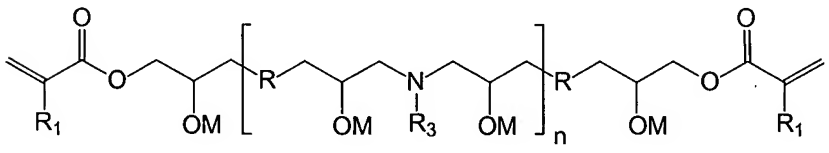

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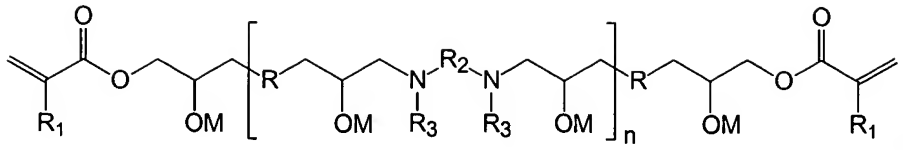

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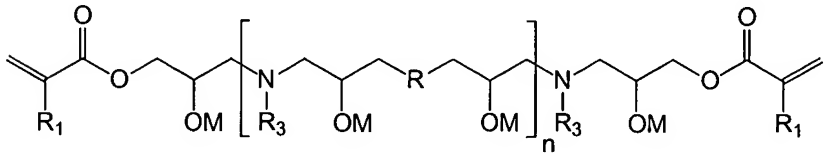

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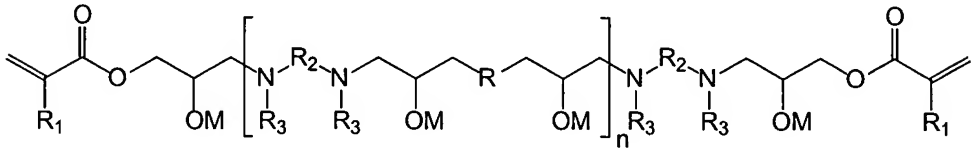

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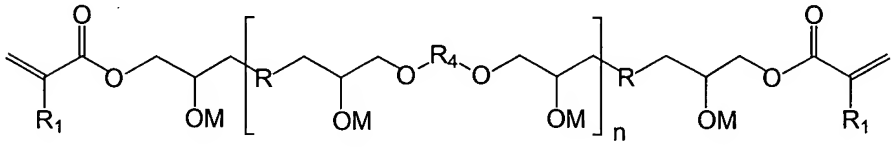

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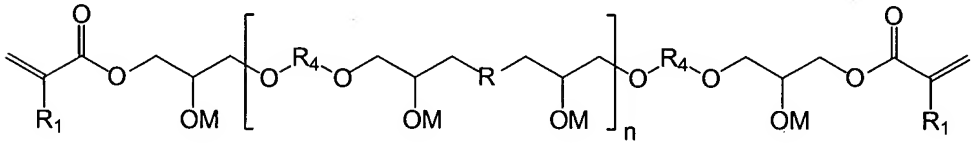

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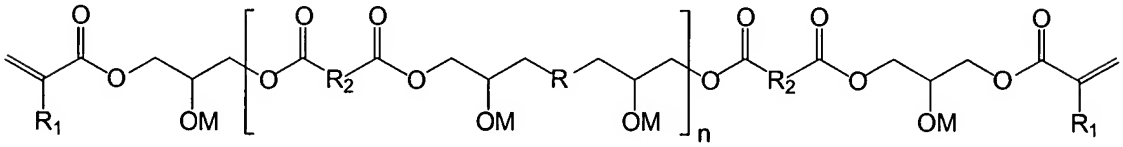

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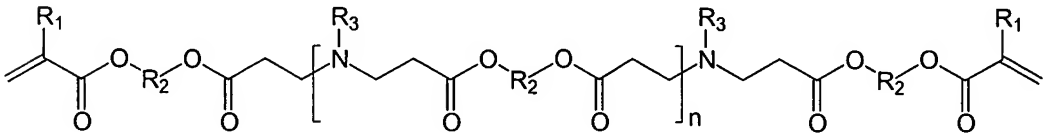

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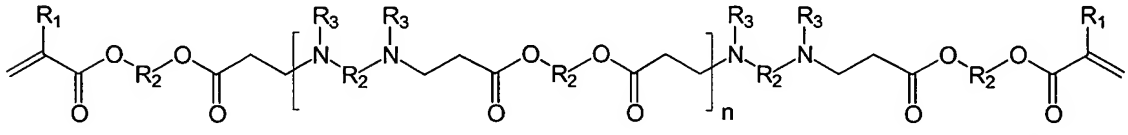

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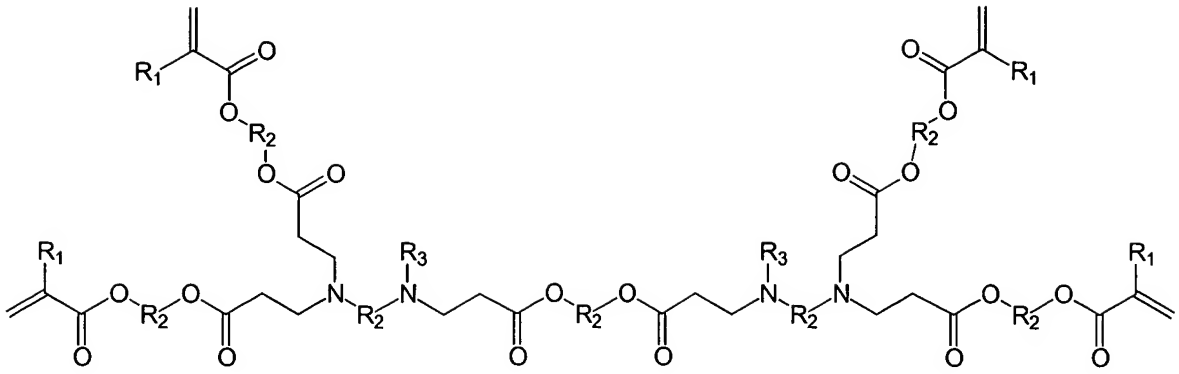

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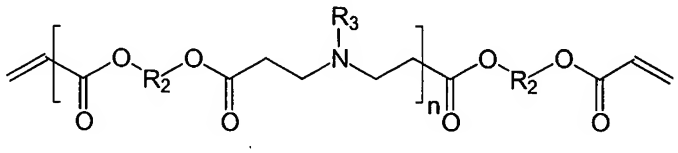

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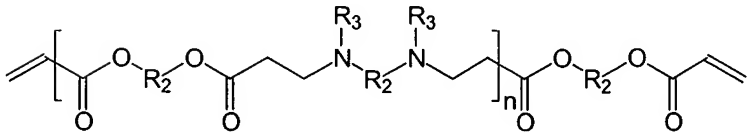

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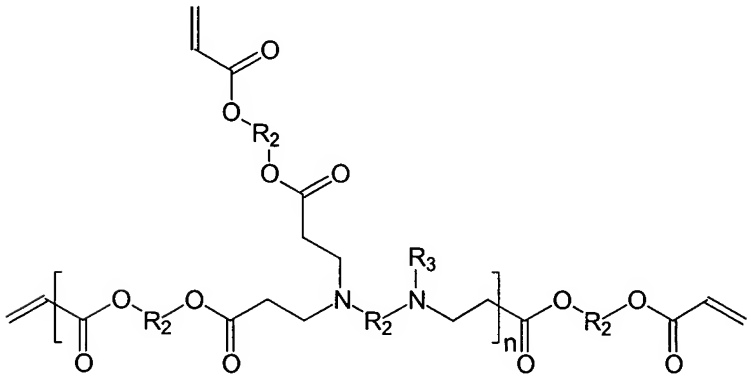

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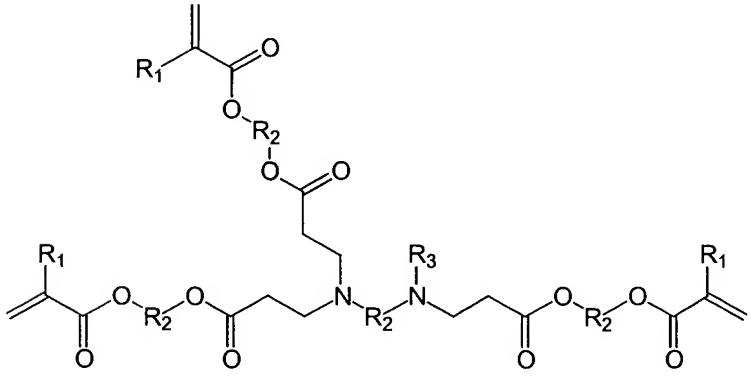

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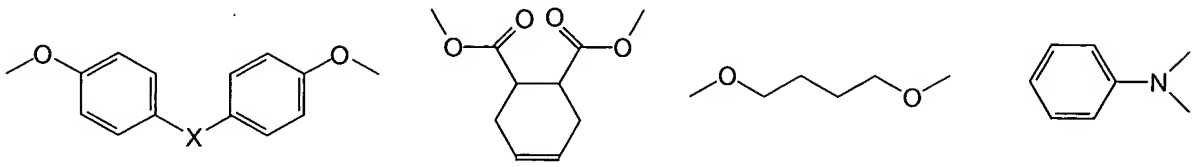
wherein

R is a residue derived from a diepoxide, notably a residue of the following formula

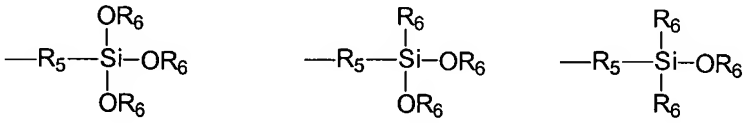


whereby X is $C(CH_3)_2$, $-CH_2-$, -O-, -S-, -CO-, $-SO_2-$

R_1 denotes hydrogen or a substituted or unsubstituted C_1 to C_{18} alkyl, C_5 to C_{18} substituted or unsubstituted cycloalkyl, substituted or unsubstituted C_5 to C_{18} aryl or heteroaryl,

R_2 is a difunctional substituted or unsubstituted C_1 to C_{18} alkylene, C_2 to C_{12} alkenyl, C_5 to C_{18} substituted or unsubstituted cycloalkylene, C_5 to C_{18} arylene or heteroarylene,

R_3 denotes a substituted or unsubstituted C_1 to C_{18} alkyl, C_2 to C_{12} alkenyl, C_5 to C_{18} substituted or unsubstituted cycloalkyl, C_6 to C_{12} aryl or C_7 to C_{12} aralkyl, or a siloxane moiety I, II or III

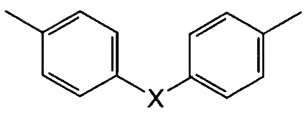
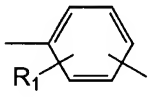


I II III

R_5 is a difunctional substituted or unsubstituted C_1 to C_{18} alkylene, C_2 to C_{12} alkenyl, C_5 to C_{18} substituted or unsubstituted cycloalkylene, C_5 to C_{18} arylene or heteroarylene, preferably $CH_2CH_2CH_2$,

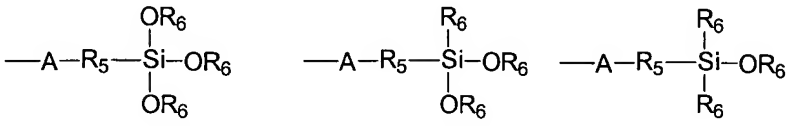
R_6 denotes a substituted or unsubstituted C_1 to C_{18} alkyl, C_2 to C_{12} alkenyl, substituted or unsubstituted C_1 to C_{18} alkylenoxy, C_5 to C_{18} substituted or unsubstituted cycloalkyl, C_6 to C_{12} aryl or C_7 to C_{12} aralkyl,

R_4 is a substituted or unsubstituted C_6 to C_{12} arylene, such as

wherein X is $C(CH_3)_2$, $-CH_2-$, -O-, -S-, -CO-, $-SO_2-$,

M is a siloxane moiety I, II or III or it is a protection groups for hydroxylic moieties such as an ether, an ester or an urethane group,



IV V IV

wherein A is an ether, an ester or an urethane linking group,

R_5 is a difunctional substituted or unsubstituted C_1 to C_{18} alkylene, C_2 to C_{12} alkenyl, C_5 to C_{18} substituted or unsubstituted cycloalkylene, C_5 to C_{18} arylene or heteroarylene,

R_6 denotes a substituted or unsubstituted C_1 to C_{18} alkyl, C_2 to C_{12} alkenyl, substituted or unsubstituted C_1 to C_{18} alkylenoxy, C_5 to C_{18} substituted or unsubstituted cycloalkyl, C_6 to C_{12} aryl or C_7 to C_{12} aralkylene,

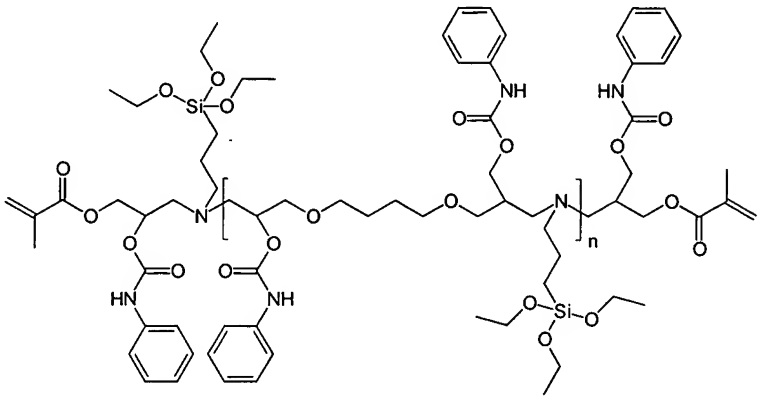
and n is an integer.

[0014] Preferably macromonomers **1** to **3** and **6** to **8** are synthesized in presence of catalysts in substance or in solvents such as THF, toluene, triethyleneglycole bismethacrylate at temperatures between 60 and 100°C.

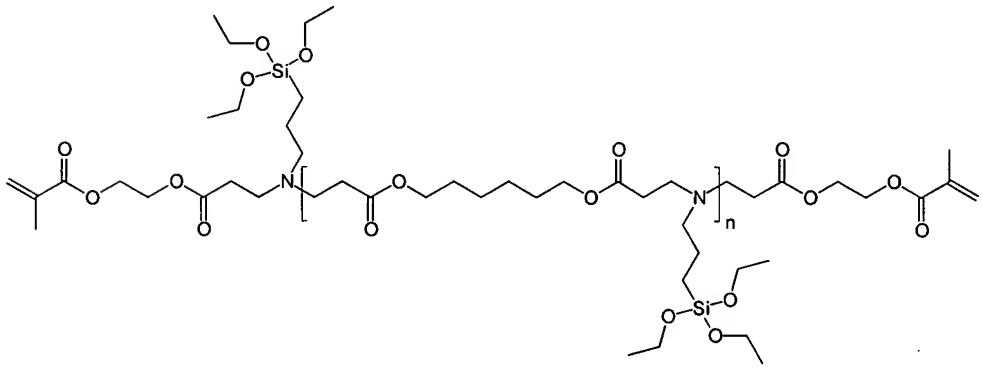
[0015] The reaction of macromonomers **4**, **5** and **9 - 15** do not require catalysts and occur commonly at 20 to 80 °C.

[0016] Maromonomers usable in dental/medical compositions comprising at least a macromonomer containing alkylsilyl, alkoxysilyl-, arylsilyl and/or aryloxysilyl groups, a polymerizable monomer, an organic or inorganic acid or a monomer that has at least an acidic moiety, a stabilizer, an initiator, pigments and an organic and/or inorganic filler.

[0017] For example a dental/medical composition comprise a macromonomer that is characterized by the following formulas:



4B-Si



9-Si

[0018] The polymerizable monomer of the dental/medical compositions is a mono- and polyfunctional (meth)-acrylate, such as a polyalkylenoxide di- and poly-(meth)acrylate, an urethane di- and poly(meth) acrylate, a vinyl-, vinylen- or vinyliden-, acrylate- or methacrylate; preferably were used diethyleneglycol dimethacrylate, triethyleneglycol dimethacrylate, 3,(4),8,(9)-dimethacryloyloxymethyltricyclodecane, dioxolan bismethacrylate, glycerol trimethacrylate, furfuryl methacrylate in a content of 5 to 80 wt-%.

[0019] Dental/medical compositions contains a polymerization initiator is a thermal initiator, a redox-initiator or a photo initiator.

[0020] Furthermore, a dental/medical composition contains a filler that preferably is an inorganic filler and/or an organic filler in an amount of 20 to 85 % (w/w).

[0021] In order to avoid spontaneous polymerization a dental/medical composition contains a stabilizer, that preferably is a radical absorbing monomer such as hydrochinon monomethylether, hydrochinon dimethylether, BHT, phenothiazine.

[0022] Due to the siloxane moieties in macromonomers a second polymerization reaction occurs using an organic or inorganic acid as a catalyst. Preferably as organic acids p-toluene sulfonic acid and ascorbic acid are used. The preferred inorganic acids are sulfuric acid or phosphoric acid or organic derivatives of them. Most preferably pentaerythrol triacrylate monophosphate and dipentaerythol pentaacrylate monophosphate are used.

[0023] Furthermore, the macromonomers are usable for filler surface modification[CW6]. When the macromonomers are used the surface modification of the glass is carried out in an organic solvent such as acetone, THF or toluene or in the absence of any solvents. The surface modification is catalyzed by amines such as primary amines, primary tertiary amines primary secondary amines, secondary amines or tertiary amines or mixtures thereof. Preferably, as catalyst aminopropy triethoxysilane, 2-aminoethyl aminopropyl triethoxysilane or triethylamine are used.

[0024] The new macromonomers are useable as precursors for siloxane condensation products, too. These condensation products containing siloxane linkages and active polymerizable moieties are usable as monomers for dental materials. Furthermore, the new hybrid monomers are usable as precursor for the preparation of nanoparticles containing active polymerizable moieties.

[0025] The invented α,ω-methacrylate terminated macromonomers **1** to **9 - 15** or the obtained gels can polymerized using photochemical and radical initiated polymerization. The obtained networks show good mechanical properties, a good adhesion to surfaces of metals, glass and ceramics. Furthermore they show a relative low water absorption. Advantageously is the relative low shrinkage during the polymerization.

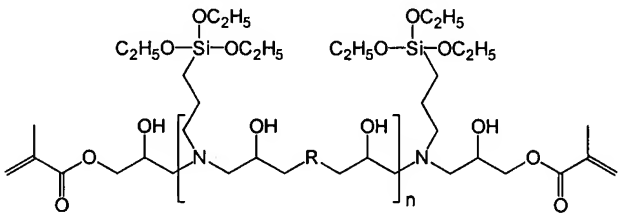
Example 1

[0026] 40.000 g (117.50 mmol) bis-[4-(2,3-epoxypropoxy)phenyl]propane, 52.023 g (235.00 mmol) 3-aminopropyl triethoxysilan, 33.408 g 2,3-

(epoxypropoxy) methyl methacrylate and 0.126 g 2,6-di-tert.-butyl-p-cresol were reacted for four hours at 90°C. The obtained methacrylate terminated macromonomer is soluble in organic solvents such as chloroform, DMF and THF. In the IR-spectrum was observed no absorption of epoxide groups at 915 and 3050 cm^{-1}. New absorption's was found at 1720 cm^{-1} (ester groups) and 3400 cm^{-1} (OH group).

M_n(vpo) = 1050 g/mol, T_g = 5.0 °C, $\eta_{(23°C)}$ = 50.4 Pa*s

($C_{53}H_{90}O_{16}N_2Si_2$), 1067.49 g/mol



4A-Si (n=1)

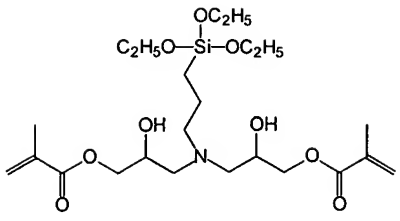
Condensation of -Si(OC_2H_5)$_3$ groups

[0027] To 16.570 g (15.52 mmol) of macromonomer **4A-Si** (n=1) dissolved in 80 ml THF were added 0.419 g (23.28 mmol) of water under stirring. The reaction mixture were stirred for additional 20 hours at ambient temperature. Then the solvent and ethanol were removed in vacuum and the condensation product was dried at 40 °C at 10 mbar.

Example 2

[0028] 50.000 g (225.9 mmol) 3-aminopropyl triethoxy silan, 64.218 g (451.7 mmol) 2,3-(epoxypropoxy) methyl methacrylate and 0.1144 g 2,6-di-tert.-butyl-p-cresol were reacted for four hours at 90°C. The obtained methacrylate terminated macromonomer is soluble in organic solvents such as chloroform, DMF and THF. In the IR-spectrum was observed no absorption of epoxide groups at 915 and 3050 cm^{-1}. New absorption's was found at 1720 cm^{-1} (ester groups) and 3400 cm^{-1} (OH group).

($C_{23}H_{43}O_9NSi$), 505.68 g/mol; $\eta_{(23°C)}$ = 34 mPa*s



4A-Si (n=0)

Condensation of -Si(OC_2H_5)$_3$ groups

[0029] To 19.260 g (38.09 mmol) of macromonomer **4A-Si** (n=0) dissolved in 80 ml THF were added 1.029 g (57.13 mmol) of water under stirring. The reaction mixture were stirred for additional 20 hours at ambient temperature. Then the solvent and ethanol were removed in vacuum and the condensation product was dried at 40 °C at 8 mbar.

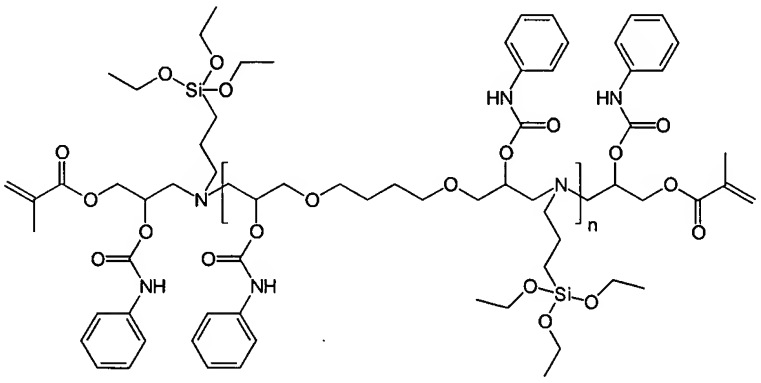
Example 3

[0030] A mixture of 50.000 g (0.247 mol) butanediole diglycidylether, 70.289 g (0.494 mol) 2,3-(epoxypropoxy) methyl methacrylate, 109.454 g (0.494 mol) 3-aminopropyltriethoxysilane and 0.230 g 2,6-di-tert.-butyl-p-cresol were reacted for 16 hours at 60°C

Yield: 229.97 g (100 %)

[0031] To 93.052 g (0.100 mol) of the reaction product were added drop-wise under stirring and cooling 47.750 g (0.401 mol) phenylisocyanate and 0.141 g di-tert.-butylsulfide.

Yield: 140.94 g (100 %)



4B-Si

[0032] In the IR spectrum of the modified macromonomer **4B-Si** absorption's at 3325 (NHCO), 1713 (CO), 1600 cm^{-1} (Ph) were found. Absorption's of OH groups at 3425 and NCO groups at 2272 cm^{-1} are completely missing.

Example 4

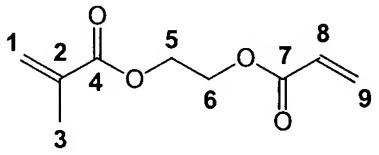
Synthesis of ethyleneglycolacrylatmethacrylat (EGAMA)

[0033] In a three-necked bottle equipped with a stirrer, a thermometer and a dropping funnel a mixture of 143.80 g (1.105 mol) of 2-hydroxyethyl methacrylate and 123.00 g (1.216 mol) of triethylamine were dissolved in 800 ml of toluene. Under cooling (0 - 5 °C) 110.00 g (1.216 mol) of acryloyl chloride dissolved in 100 ml toluene were added during four hours. After standing over night, the precipitate was filtered off and washed twice with 20 ml of toluene. Then the reaction mixture was extracted twice with 200 ml water, with 150 ml 1 n HCl and with 150 ml 1 n $NaHCO_3$ and dried over $NaSO_4$. Thereafter the toluene was distilled off at 32 mbar and 40 °C and 0.2035g BHT were added.

Yield: 156.71g (77 % of th.); bp. 70°C/ 8 mbar, n_D^{20} = 1.4530

^1H NMR ($CDCl_3$)/ppm: 5.48 / 6.30 (1), 1.72 (3), 4.28 (5, 6), 5.73 (8), 6.03 (9)

^{13}C NMR ($CDCl_3$)/ppm: 126.0 (1), 135.8 (2), 17.6 (3), 165.6 (4), 62.2 (5, 6), 167.1 (7), 128.0 (8), 131.1 (9)



Macromonomer **9-Si (n=0)**:

[0034] 20.232 g (109.8 mmol) EGAMA, 12.158 g (54.9 mmol) aminopropyl triethoxysilane and 0.032 g BHT were mixed homogeneously and stirred at room temperature for 12 hours.

$C_{27}H_{47}NO_{11}Si$, 589.75 g/mol; m/z (FAB-MS) = 590.

Condensation of $-Si(OC_2H_5)_3$ groups

[0035] To 12.000 g (11.57 mmol) of macromonomer 9-Si dissolved in 50 ml THF were added 0.313 g (17.35 mmol) of water under stirring. The reaction

mixture were stirred for additional 20 hours at ambient temperature. Then the solvent and ethanol were removed in vacuum and the condensation product was dried at 40 °C at 8 mbar.

Example 5 (Macromonomer 9-Si, n=1)

[0036] 24.643 g (133.8 mmol) EGAMA and 0.062 g BHT were dissolved in 100 ml methanol. To this mixture 25.600 g (133.8 mmol) aminopropyl triethoxysilane were added at 0 - 5 °C and stirred for 2 hours. Then the methanol was distilled off and the mixture was reacted for a further 24 hours at 23 °C.

$C_{42}H_{76}N_2O_{16}Si_2$, 921.24 g/mol

Example 6 (Macromonomer 15-Si)

[0037] 26.777 g (145.4 mmol) EGAMA, 10.000 g (48.5 mmol) 2-aminoethyl aminopropyl methyl dimethoxysilane and 0.037 g BHT were mixed homogeneously and stirred at room temperature for 12 hours.

$C_{35}H_{58}N_2O_{14}Si$, 758.93 g/mol; m/z (FAB-MS) = 759, n_D^{20} = 1.4749, $\eta_{(23°C)}$ = 144 Pa*s.

Application Example 7 – Filler surface modification

[0038] 3-aminopropyl-methyl-diethoxysilane/EGAMA adduct

In a three-necked flask with a dropping funnel, dimroth cooler, $CaCl_2$-drying tube, thermometer and magnetic stirrer 79.956 g (434.1 mmol) EGAMA and 0.121 g BHT are dissolved in 210 ml THF. At a temperature of 0-5°C 41.530 g aminopropyl methyl-diethoxysilane in 25 ml THF are added by dropping over a period of 60 min. Afterwards the solution is stirred at room temperature for additional four hours. The solvent is evaporated under reduced pressure of 8 mmbar and a bath temperature of 40°C. The remaining mixture is stirred for additional 24 h at 23°C and 5 hours at 40°C. The addition product APDES/EGAMA was characterized by FAB-MS m/z 560, n_D^{20} = 1.4600, $\eta_{(23°C)}$ = 40 mPa*s.

$C_{26}H_{45}NO_{10}Si$, 559.72 g/mol.

[0039] Modified inorganic glass filler (3.0 %):

50 g of an barium alumo silicate glass having a particle size of 0.9 – 1.5 µm is dispersed in 250 ml of acetone. 1.5 g of the adduct of 3-aminopropyl-methyl-diethoxysilane/EGAMA is added, 2.0 g of diethylamine and 1.0 g of water are added to the dispersion. The dispersion is stirred at 60° for 6 h. The solvent is evaporated. For the silanation the remaining solid is stored at 115° for 15 – 18 h under reduced pressure (20 mbar) and sieved through a 220 µm sieve.

[0040] To control the success of the silanation a part of the silanated glass was stirred in acetone for 5 h. The solvent was filtered. The remaining glass was washed with acetone. The solutions were dried and the residue of non bonded silane on the glass was weighted.

20.2 % silane were found in the solution. The remaining 79.8 % were bond to the glass surface. Therefore the glass has a total silane content of 2.4 %

[0041] The obtained modified glass filler is used in dental/medical composite.

1. Dental/medical composite resin

28.900 g 2,2-Bis-[p-(2-hydroxy-3-methacryloyloxypropoxy)-phenyl]-propane (Bis-GMA), 31.225 g triethylene glycol dimethacrylate, 31.226 g ethoxylated bisphenol-A-dimethacrylate, 8.198 g hexamethylenediisocyanate, 0.330 g dibutyltindilaurate and 0.100 g BHT are mixed in a 250 ml beaker by stirring at 40°C.

The obtained resin is used directly for the preparation of a dental/medical composite.

Activated resin

99.35 g resin as described above, 0.30 g camphor quinone and 0.35 DMABE are mixed in a 250 ml beaker by stirring at 40°C.

2. Dental/medical composite

240 g activated resin as described above are mixed with 760 g of modified inorganic glass filler as described above by the use of an planetary mixer under exclusion of daylight. The glass is successively added in five steps of 400 g, 150 g, 100, 50 g and 50 g. After getting a homogeneous paste the

mixture is evaporated at a pressure of 180 – 220 mbar. For conditioning the paste is stored under exclusion of daylight for additional 24 h at 40°C.

3. Properties of dental/medical composites

Dental/medical composites obtained according the method described above were tested on their mechanical properties on a standard testing machine (Zwick Z 010). The compressive strength was measured according to the ISO standard 9917, 1991 (dental water based cements), the flexural strength was measured according to ISO 4049, 1988 (dental composite materials).

The consistency of the composites were measured as following: To portion 0,5 ml of the composite it is filled into a cylindrical hole of a diameter of 0,7 ml and a height of 1,3 mm. The composite is dosed on a surface of a polyetherketone foil and load with a weight of 575 g over a period of 30 sec. Afterwards the diameter of the obtained composite circle is measured in mm and noted as the consistency of the material.

[0042] The volumetric shrinkage is measured in two different ways. According to the Archimedes method by measuring the change of the density as a result of the polymerization reaction and by measuring the linear dimensional change after the polymerization. The linear dimensional change was afterwards calculated to a volumetric shrinkage (ZH-method).

All results are shown in the table below.

		MS-8.125.1	MS-8.125.2	MS-8.130.1
Type of silane		EGAMA-APDES	EGAMA-APDES	A-174
Silane content on glass	%	2.5	4.0	3.0
Filler content	%	75.0	76.2	75.0
Compr. strength	MPa	287.1 ± 20.9	282.5 ± 12.3	349.5 ± 9.7
Flexural strength	MPa	103.4 ± 11.2	101.7 ± 4.3	126.3 ± 11.3
E-Modulus	MPa	7381 ± 300	6948 ± 700	-
Volumetric shrinkage (Archimedes-method)	%	3.21 ± 0.09	3.31 ± 0.06	3.00 ± 0.48
Volumetric shrinkage (ZH-method)	%	1.38 ± 0.20	1.33 ± 0.11	1.63 ± 0.14
Consistency	mm	10.5	11.0	10.0

Application Example 8 – Condensation to nanoparticles in TGDMA

[0043] 1g (1,8 mmol) addition product of EGAMA and aminopropyl trimethoxysilane were dissolved in 9 g TGDMA. To this solution were added 0,15 g (8,2 mmol) water. Then this mixture and stirred for 14 days at room temperature. The formed particles have an average particle size of 3 nm. The Transmission electron microscopic photograph (**Error! Reference source not found.**) show the formed nano-scaled particles. In the IR spectrum double bonds of the methacrylate groups were found at 1720 cm^{-1}.

Application Example 9 – Condensation to nanoparticles

[0044] 1g (1,8 mmol) addition product of EGAMA and aminopropyl trimethoxysilane were dissolved in 10 ml ethanol. To this solution were added 1.08 g water and 0.51 g of acetic acid and stirred for 14 days at room temperature. The formed particles have an average particle size of 6.6 nm.

[0045] In the Element specific image of the Transmission electron microscopic photograph (**Error! Reference source not found.**) the silcium atoms of nano-scaled particles were found. These particles were observed in the Transmission electron microscopic photograph (**Error! Reference source not found.**), too. In the IR spectrum double bonds of the methacrylate groups were found at 1720 cm^{-1}.

Application Example 9 - Preparation a composite

[0046] 0.035g camphor quinone and 0.035g dimethylamino benzoic acid ethyl ester were added to 3.00g of the addition product of EGAMA and aminopropyl diethoxymethylsilane and 7.00 g Bis-GMA. To this mixture silanized Spectrum glass (Schott) was added so that composites with about 70% share filler were obtained. Then the composite was homogenized by stirring at 40°C for 30 min and then degassed at 200 mbar and 60°C for 15 min. The photochemical polymerization of these samples was carried out in a Triad photochemical curing unit (Dentsply De Trey, Konstanz) within 4 minutes.

[0047] The composite shows a compressive strength of 291.3 MPa a flexural strength of 53 MPa and an E-modulus of 3830 MPa. The volumetric shrinkage is 1.79 % at an degree of conversion of 0.86 (measured by using of DSC).